(FILE 'HOME' ENTERED AT 16:35:37 ON 15 OCT 2003)

FILE 'REGISTRY' ENTERED AT 16:35:52 ON 15 OCT 2003
E "TRIACETYLURIDINE"/CN 25
E "2',3',5'-TRI-O-ACETYLURIDINE"/CN 25
L1 1 S E3

FILE 'CAPLUS, MEDLINE, USPATFULL, EUROPATFULL' ENTERED AT 16:38:44 ON 15 OCT 2003
L2 206 S L1
L3 4 S L2 AND RESPIRATORY CHAIN DYSFUNCTION
L4 3 S L3 AND CREATINE
L5 0 S ACETYURIDINE
L6 232 S ACETYLURIDINE
L7 344 S ?ACETYLURIDINE
L8 46 S L7 AND (MELAS OR LHON OR MERRF OR MNGIE OR NARP OR PEO OR LE
L9 15 S L8 AND CREATINE

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  (FILE 'HOME' ENTERED AT 16:35:37 ON 15 OCT 2003)

     FILE 'REGISTRY' ENTERED AT 16:35:52 ON 15 OCT 2003
               E "TRIACETYLURIDINE"/CN 25
               E "2',3',5'-TRI-O-ACETYLURIDINE"/CN 25
L1           1 S E3

     FILE 'CAPLUS, MEDLINE, USPATFULL, EUROPATFULL' ENTERED AT 16:38:44 ON 15
     OCT 2003
L2         206 S L1
L3           4 S L2 AND RESPIRATORY CHAIN DYSFUNCTION
L4           3 S L3 AND CREATINE

=>
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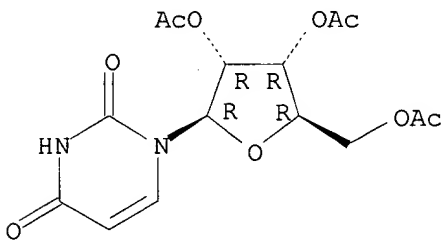
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 4105-38-8 REGISTRY
CN Uridine, 2',3',5'-triacetate (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN **2',3',5'-Tri-O-acetyluridine**
CN 2',3',5'-Triacetyluridine
CN Tri-O-acetyl uridine
FS STEREOSEARCH
DR 293738-13-3
MF C15 H18 N2 O9
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DRUGUPDATES, HODOC*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

172 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
172 REFERENCES IN FILE CAPLUS (1907 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 1 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2002:92658 USPATFULL

TITLE: Compositions and methods for treatment of mitochondrial diseases

INVENTOR(S): Von Borstel, Reid W., Potomac, MD, UNITED STATES
Saydoff, Joel A., Middletown, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002049182	A1	20020425
APPLICATION INFO.:	US 2001-930494	A1	20010816 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-763955, filed on 28 Feb 2001, PENDING A 371 of International Ser. No. WO 1999-US19725, filed on 31 Aug 1999, UNKNOWN Continuation-in-part of Ser. No. US 1998-144096, filed on 31 Aug 1998, PENDING

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: NIXON & VANDERHYE P.C., 8th Floor, 1100 North Glebe Road, Arlington, VA, 22201

NUMBER OF CLAIMS: 50

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 16 Drawing Page(s)

LINE COUNT: 2171

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . of the invention to provide compositions and methods for treating disorders or pathophysiological consequences associated with mitochondrial dysfunction or mitochondrial **respiratory chain dysfunction** in a mammal, including a human.

DRWD [0033] FIG. 1: Survival plot of mice treated with 3NP in addition to TAU and/or **creatine**.

DRWD [0036] FIG. 4: The effect of 3NP and TAU and/or **creatine** on body weight as a percentage of baseline body weight. * Indicates $p<0.05$ difference compared to the Vehicle+Vehicle treatment group.

DRWD [0039] FIG. 7: The effect of 3NP and TAU and/or **creatine** on activity. There was a difference for the TAU+3NP and **Creatine** +3NP groups compared to the Vehicle+Vehicle treatment group of $p<0.001$.

DRWD [0042] FIG. 10: The effect of 3NP with TAU and/or **creatine** on rotarod performance at 5 RPM. There was a $p<0.01$ difference compared to the Vehicle+Vehicle treatment group compared to the Vehicle+3NP or **Creatine**+3NP groups.

DRWD [0043] FIG. 11: The effect of 3NP with TAU and/or **creatine** on rotarod performance at 10 RPM. There was a $p<0.05$ difference compared to the Vehicle+Vehicle treatment group compared to the. . .

DETD . . . acid, pyruvic acid, lactic acid, enolpyruvic acid, lipoic acid, pantothenic acid, acetoacetic acid, p-aminobenzoic acid, betahydroxybutyric acid, orotic acid, and **creatine**.

DETD . . . acid, pyruvic acid, lactic acid, enolpyruvic acid, lipoic acid, pantothenic acid, acetoacetic acid, p-aminobenzoic acid, betahydroxybutyric acid, orotic acid, and **creatine**.

DETD . . . alone, without coadministration of a pyrimidine nucleotide precursor, for the purpose of treating mitochondrial diseases or pathophysiologies associated with mitochondrial **respiratory chain dysfunction**.

DETD . . . niacin (20 to 100 mg/day), Vitamin C (100 to 1000 mg/day), Vitamin E (200-400 mg/day), dichloroacetic acid or its salts, **creatine** (1 to 200 g/day, preferably 1 to 50 g/day). (The recommended daily doses given in the previous sentence are for. . .

DETD [0109] Diseases related to mitochondrial **respiratory chain dysfunction** can be divided into several categories based on the origin of mitochondrial defects.

DETD Pathophysiological Consequences of **Respiratory Chain Dysfunction**

DETD . . . cells. Nondividing tissues with high energy requirements, e.g. nervous tissue, skeletal muscle and cardiac muscle are particularly susceptible to mitochondrial **respiratory chain dysfunction**, but any organ system can be affected.

DETD [0121] The diseases and symptoms listed below comprise known pathophysiological consequences of mitochondrial **respiratory chain dysfunction** and as such are disorders in which the compounds and compositions of the invention have therapeutic utility.

DETD . . . necessarily yield symptoms under normal conditions. Neuromuscular or neurological setbacks during infection are a hallmark of mitochondrial disease. Conversely, mitochondrial **respiratory chain dysfunction** can render cells vulnerable to stressors that would otherwise be innocuous.

DETD . . . of respiratory chain complex activity in fresh tissue samples) with a good degree of certainty in establishing the role of **respiratory chain dysfunction** in disease pathogenesis, and a larger number of minor criteria (e.g. moderate biochemical abnormalities characteristic of respiratory chain defects, symptoms. . .

DETD . . . both diseases, factors which both exacerbate mitochondrial respiratory chain deficits and whose deleterious actions are exaggerated on a background of **respiratory chain dysfunction**.

DETD [0168] Acidosis due to renal dysfunction is often observed inpatients with mitochondrial disease, whether the underlying **respiratory chain dysfunction** is congenital or induced by--ischemia or cytotoxic agents like cisplatin. Renal tubular acidosis often requires administration of exogenous sodium bicarbonate. . .

DETD . . . mg/kg/day, again depending on the amount needed to achieve an optimal therapeutic effect in a particular disease state involving mitochondrial **respiratory chain dysfunction** . The dose of pyrimidine nucleotide precursor of the invention required for a particular disease or patient will also depend in. . .

DETD Effect of TAU Coadministered with **Creatine** or Coenzyme Q10 in 3NP Model of Huntingdon's Disease

DETD PN401, **Creatine** or Coenzyme Q10 Administration

DETD . . . Division, 5-1, Nihonbashi-Kobunacho, Chuo-Ku, Tokyo 103, Japan; Lot 103 H 0060) was mixed into the rodent chow at 6% weight/weight. **Creatine** (Sigma) was mixed into the chow at 2% (weight/weight) that is previously reported to be the optimal dose (Matthews, Yang. . .

DETD [0246] **Creatine**+3NP

DETD [0247] TAU and **Creatine**+Vehicle

DETD [0265] TAU and/or coenzyme Q10 (but not **creatine**) decreased mortality due to 3NP treatment (FIGS. 1 and 2). TAU dose-dependently decreased mortality with 4 and 8% TAU decreasing. . .

DETD [0266] In experiments 1-3, 3NP significantly decreased body weight (FIGS. 4-6). TAU or TAU+**creatine** attenuated (not significant $p<0.05$) the loss of body weight. In experiment 2, 3NP also lead to a significant decrease in. . .

DETD . . . there was a significant ($p<0.001$) decrease in activity due 3NP treatment that was not attenuated by treatment with TAU or **creatine**, but was blocked when TAU and **creatine** were combined indicating a strong positive interaction between these 2 compounds (FIG. 7).

DETD [0270] In experiment 1, rotarod performance at 5 RPM was significantly ($p<0.01$) impaired due to 3NP treatment (FIG. 10). The **creatine** +3NP group was also significantly ($p<0.01$) compared to the Vehicle+Vehicle control group. PN401 or TAU/**creatine** treatment prevented significant impairment due to 3NP.

CLM What is claimed is:

1. A method for treating or preventing pathophysiological consequences of mitochondrial **respiratory chain**

dysfunction in a mammal comprising administering to said mammal in need of such treatment or prevention an effective amount of a. . .

2. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by a mutation, deletion, or rearrangement of mitochondrial DNA.

3. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by defective nuclear-encoded protein components of the mitochondrial respiratory chain.

4. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by aging.

5. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by administration of cytotoxic cancer chemotherapy agents to said mammal.

6. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex I activity.

7. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex II activity.

8. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex III activity.

9. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex IV activity.

10. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex V activity.

21. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a congenital mitochondrial disease.

23. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a neurodegenerative disease.

28. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a neuromuscular degenerative disease.

30. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is developmental delay in cognitive, motor, language, executive function, or social skills.

31. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is selected from the group consisting of epilepsy, peripheral-neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic bladder. . .

32. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is selected from the group consisting of renal

tubular acidosis, dilating cardiomyopathy, steatohepatitis, hepatic failure, and lactic acidemia.

33. A method for preventing death or functional decline of post-mitotic cells in a mammal due to mitochondrial **respiratory chain dysfunction** comprising administration of an effective amount of a pyrimidine nucleotide precursor.

48. A method as in claim 1 further comprising administering to the mammal an amount of **creatine** such that the combined amount of **creatine** and the pyrimidine nucleotide is effective to treat said consequences of mitochondrial **respiratory chain dysfunction**.

50. A pharmaceutical composition comprising: (a) a pyrimidine nucleotide precursor or a pharmaceutically acceptable salt thereof, and (b) **creatine**.

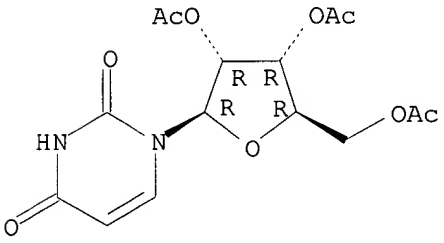
IT 58-96-8, Uridine 65-46-3, Cytidine 65-86-1, Orotic acid 65-86-1D, Orotic acid, esters 127-17-3D, Pyruvic acid, esters 303-98-0, Coenzyme Q10 987-78-0, Cytidine diphosphocholine 1747-53-1, Ethyl orotate **4105-38-8**, 2',3',5'-Tri-O-acetyluridine 260360-02-9 260360-03-0 260360-04-1 260360-05-2 260360-06-3 260360-07-4
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT **4105-38-8**, 2',3',5'-Tri-O-acetyluridine
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

RN 4105-38-8 USPATFULL

CN Uridine, 2',3',5'-triacetate (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER:	2001:139534 USPATFULL
TITLE:	Compositions and methods for treatment of mitochondrial diseases
INVENTOR(S):	von Borstel, Reid W., Potomac, MD, United States
PATENT ASSIGNEE(S):	Pro-Neuron, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001016576	A1	20010823
APPLICATION INFO.:	US 2001-838136	A1	20010420 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-144096, filed on 31 Aug 1998, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Nixon & Vanderhye P.C., 8th Floor, 1100 N. Glebe Rd., Arlington, VA, 22201		
NUMBER OF CLAIMS:	46		
EXEMPLARY CLAIM:	1		

LINE COUNT: 1390
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . object of the invention to provide compositions and methods for treating disorders or pathophysiology associated with mitochondrial dysfunction or mitochondrial **respiratory chain dysfunction** in a mammal, including a human.

DETD . . . acid, pyruvic acid, lactic acid, enolpyruvic acid, lipoic acid, pantothenic acid, acetoacetic acid, p-aminobenzoic acid, betahydroxybutyric acid, orotic acid, and **creatine.**

DETD . . . acid, pyruvic acid, lactic acid, enolpyruvic acid, lipoic acid, pantothenic acid, acetoacetic acid, p-aminobenzoic acid, betahydroxybutyric acid, orotic acid, and **creatine.**

DETD . . . alone, without coadministration of a pyrimidine nucleotide precursor, for the purpose of treating mitochondrial diseases or pathophysiologies associated with mitochondrial **respiratory chain dysfunction.**

DETD [0089] Diseases related to mitochondrial **respiratory chain dysfunction** can be divided into several categories based on the origin of mitochondrial defects.

DETD . . . necessarily yield symptoms under normal conditions. Neuromuscular or neurological setbacks during infection are a hallmark of mitochondrial disease. Conversely, mitochondrial **respiratory chain dysfunction** can render cells vulnerable to stressors that would otherwise be innocuous.

DETD . . . both diseases, factors which both exacerbate mitochondrial respiratory chain deficits and whose deleterious actions are exaggerated on a background of **respiratory chain dysfunction.**

DETD [0143] Acidosis due to renal dysfunction is often observed in patients with mitochondrial disease, whether the underlying **respiratory chain dysfunction** is congenital or induced by ischemia or cytotoxic agents like cisplatin. Renal tubular acidosis often requires administration of exogenous sodium. . .

CLM What is claimed is:

1. A method for treating or preventing pathophysiological consequences of mitochondrial **respiratory chain dysfunction** in a mammal comprising administering to said mammal in need of such treatment or prevention an effective amount of a. . .

2. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by a mutation, deletion, or rearrangement of mitochondrial DNA.

3. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by defective nuclear-encoded protein components of the mitochondrial respiratory chain.

4. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by aging.

5. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by administration of cytotoxic cancer chemotherapy agents to said mammal.

6. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex I activity.

7. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex II activity.

8. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial

Complex III activity.

9. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex IV activity.

10. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex V activity.

20. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a congenital mitochondrial disease.

22. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a neurodegenerative disease.

27. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a neuromuscular degenerative disease.

29. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is developmental delay in cognitive, motor, language, executive function, or social skills.

30. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is selected from the group consisting of epilepsy, peripheral neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic. . .

31. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is selected from the group consisting of renal tubular acidosis, dilating cardiomyopathy, hepatic failure, and lactic acidemia.

32. A method for preventing death or functional decline of post-mitotic cells in a mammal due to mitochondrial **respiratory chain dysfunction** comprising administration of an effective amount of a pyrimidine nucleotide precursor.

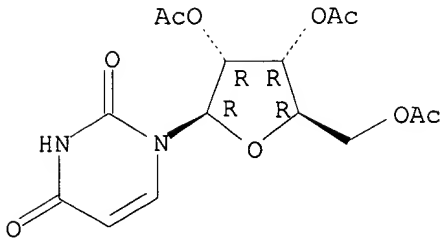
IT 58-96-8D, Uridine, acyl derivs. 65-46-3, Cytidine 65-46-3D, Cytidine, acyl derivs. 65-86-1, Orotic acid 65-86-1D, Orotic acid, esters 127-17-3, Pyruvic acid, biological studies 127-17-3D, Pyruvic acid, esters 987-78-0, Cytidine diphosphocholine 1747-53-1, Ethyl orotate **4105-38-8**, 2',3',5'-Tri-O-acetyluridine 260360-02-9 260360-03-0 260360-04-1 260360-05-2 260360-06-3 260360-07-4
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **4105-38-8**, 2',3',5'-Tri-O-acetyluridine
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

RN 4105-38-8 USPATFULL

CN Uridine, 2',3',5'-triacetate (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 3 OF 3 USPATFULL on STN

ACCESSION NUMBER:	2001:100342 USPATFULL
TITLE:	COMPOSITIONS AND METHODS FOR TREATMENT OF MITOCHONDRIAL DISEASES
INVENTOR(S):	VON BORSTEL, REID W., POTOMAC, MD, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001005719	A1	20010628
	US 6472378	B2	20021029
APPLICATION INFO.:	US 1998-144096	A1	19980831 (9)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	NIXON & VANDERHYE, 1100 N. GLEBE ROAD, 8TH FLOOR, ARLINGTON, VA, 22201
NUMBER OF CLAIMS:	46
EXEMPLARY CLAIM:	1
LINE COUNT:	1402

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . object of the invention to provide compositions and methods for treating disorders or pathophysiology associated with mitochondrial dysfunction or mitochondrial **respiratory chain dysfunction** in a mammal, including a human.

SUMM . . . acid, pyruvic acid, lactic acid, enolpyruvic acid, lipoic acid, pantothenic acid, acetoacetic acid, p-aminobenzoic acid, betahydroxybutyric acid, orotic acid, and **creatine**.

SUMM . . . acid, pyruvic acid, lactic acid, enolpyruvic acid, lipoic acid, pantothenic acid, acetoacetic acid, p-aminobenzoic acid, betahydroxybutyric acid, orotic acid, and **creatine**.

SUMM . . . alone, without coadministration of a pyrimidine nucleotide precursor, for the purpose of treating mitochondrial diseases or pathophysiologies associated with mitochondrial **respiratory chain dysfunction**.

SUMM [0087] Diseases related to mitochondrial **respiratory chain dysfunction** can be divided into several categories based on the origin of mitochondrial defects.

SUMM . . . necessarily yield symptoms under normal conditions. Neuromuscular or neurological setbacks during infection are a hallmark of mitochondrial disease. Conversely, mitochondrial **respiratory chain dysfunction** can render cells vulnerable to stressors that would otherwise be innocuous.

SUMM . . . both diseases, factors which both exacerbate mitochondrial respiratory chain deficits and whose deleterious actions are exaggerated on a background of **respiratory chain dysfunction**.

SUMM [0138] Acidosis due to renal dysfunction is often observed in patients with mitochondrial disease, whether the underlying **respiratory chain dysfunction** is congenital or induced by ischemia or cytotoxic agents like cisplatin. Renal tubular acidosis often requires administration of exogenous sodium. . .

CLM What is claimed is:

1. A method for treating or preventing pathophysiological consequences

of mitochondrial **respiratory chain dysfunction** in a mammal comprising administering to said mammal in need of such treatment or prevention an effective amount of a. . .

2. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by a mutation, deletion, or rearrangement of mitochondrial DNA.

3. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by defective nuclear-encoded protein components of the mitochondrial respiratory chain.

4. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by aging.

5. A method as in claim 1 wherein said **respiratory chain dysfunction** is caused by administration of cytotoxic cancer chemotherapy agents to said mammal.

6. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex I activity.

7. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex II activity.

8. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex III activity.

9. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex IV activity.

10. A method as in claim 1 wherein said **respiratory chain dysfunction** is a deficit in mitochondrial Complex V activity.

20. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a congenital mitochondrial disease.

22. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a neurodegenerative disease.

27. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is a neuromuscular degenerative disease.

29. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is developmental delay in cognitive, motor, language, executive function, or social skills.

30. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is selected from the group consisting of epilepsy, peripheral neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic. . .

31. A method as in claim 1 wherein said pathophysiological consequence of mitochondrial **respiratory chain dysfunction** is selected from the group consisting of renal

tubular acidosis, dilating cardiomyopathy, hepatic failure, and lactic acidemia.

32. A method for preventing death or functional decline of post-mitotic cells in a mammal due to mitochondrial **respiratory chain dysfunction** comprising administration of an effective amount of a pyrimidine nucleotide precursor.

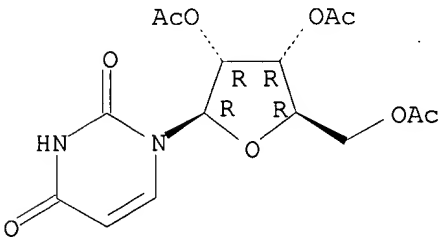
IT 58-96-8D, Uridine, acyl derivs. 65-46-3, Cytidine 65-46-3D, Cytidine, acyl derivs. 65-86-1, Orotic acid 65-86-1D, Orotic acid, esters 127-17-3, Pyruvic acid, biological studies 127-17-3D, Pyruvic acid, esters 987-78-0, Cytidine diphosphocholine 1747-53-1, Ethyl orotate **4105-38-8**, 2',3',5'-Tri-O-acetyluridine 260360-02-9 260360-03-0 260360-04-1 260360-05-2 260360-06-3 260360-07-4
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **4105-38-8**, 2',3',5'-Tri-O-acetyluridine
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

RN 4105-38-8 USPATFULL

CN Uridine, 2',3',5'-triacetate (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



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